Clinical trial results:
An Early-Phase, Multicenter, Open-Label Study of the Safety and Pharmacokinetics of Atezolizumab (MPDL3280A) In Pediatric and Young Adult Patients With Previously Treated Solid Tumors

Summary

EudraCT number	2014-004697-41
Trial protocol	DK DE IE ES FR AT NL IT
Global end of trial date	06 June 2019

Results information

Result version number	v2
This version publication date	03 January 2020
First version publication date	27 November 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	GO29664

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02541604
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland,
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001638-PIP01-14
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 June 2019
Global end of trial reached?	Yes
Global end of trial date	06 June 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the safety, tolerability, PK, pharmacodynamics, immunogenicity, and preliminary efficacy of atezolizumab administered by IV infusion every 3 weeks to pediatric and young adult patients with solid tumors for which prior treatment has proven to be ineffective (i.e., relapsed or refractory) or intolerable and for whom there is no effective standard treatment available.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 November 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	United States: 19
Worldwide total number of subjects	87
EEA total number of subjects	64

Notes:

Subjects enrolled per age group

In utero	0

Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	1
Infants and toddlers (28 days-23 months)	1
Children (2-11 years)	29
Adolescents (12-17 years)	38
Adults (18-64 years)	18
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects in this study included pediatric and young adult patients with solid tumors with known or expected PD-L1 pathway involvement for which prior treatment has proven to be ineffective (i.e., relapsed or refractory) or intolerable, and for whom no curative standard-of-care treatment options exist.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	COHORT 1 (EWING SARCOMA)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle

Arm title	COHORT 2 (HODGKIN LYMPHOMA)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle

Arm title	COHORT 3 (NEUROBLASTOMA)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle

Arm title	COHORT 4 (NON HODGKIN LYMPHOMA)

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle	
Arm title	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle	
Arm title	COHORT 6 (OSTEOSARCOMA)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle	
Arm title	COHORT 7 (RHABDOMYOSARCOMA)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle	
Arm title	COHORT 8 (WILMS TUMOR)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle	
Arm title	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1

	EXPRESSION)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle	
Arm title	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)
Arm description: OTHER TUMOR TYPES WITHOUT DOCUMENTED PD-L1 EXPRESSION	
Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle	
Arm title	COHORT 11 (RHABDOID TUMOR)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle	
Arm title	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: IV infusion (maximum 1200 mg) on Day 1 of each 21-day cycle	

Number of subjects in period 1	COHORT 1 (EWING SARCOMA)	COHORT 2 (HODGKIN LYMPHOMA)	COHORT 3 (NEUROBLASTOMA)
Started	11	9	11
Completed	0	0	0
Not completed	11	9	11
Consent withdrawn by subject	2	-	1
Death	6	5	7
Study Terminated by Sponsor	1	4	2
Lost to follow-up	2	-	1
Medical condition may jeopardize safety	-	-	-

Number of subjects in period 1	COHORT 4 (NON HODGKIN LYMPHOMA)	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)	COHORT 6 (OSTEOSARCOMA)
Started	3	10	10
Completed	0	0	0
Not completed	3	10	10
Consent withdrawn by subject	-	1	1
Death	2	9	8
Study Terminated by Sponsor	1	-	-
Lost to follow-up	-	-	1
Medical condition may jeopardize safety	-	-	-

Number of subjects in period 1	COHORT 7 (RHABDOMYOSARCOMA)	COHORT 8 (WILMS TUMOR)	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)
Started	10	10	4
Completed	0	0	0
Not completed	10	10	4
Consent withdrawn by subject	-	-	1
Death	9	9	3
Study Terminated by Sponsor	-	-	-
Lost to follow-up	1	-	-
Medical condition may jeopardize safety	-	1	-

Number of subjects in period 1	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)	COHORT 11 (RHABDOID TUMOR)	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)
Started	4	2	3
Completed	0	0	0
Not completed	4	2	3
Consent withdrawn by subject	-	-	-
Death	4	2	3

Study Terminated by Sponsor	-	-	-
Lost to follow-up	-	-	-
Medical condition may jeopardize safety	-	-	-

Baseline characteristics

Reporting groups	
Reporting group title	COHORT 1 (EWING SARCOMA)
Reporting group description: -	
Reporting group title	COHORT 2 (HODGKIN LYMPHOMA)
Reporting group description: -	
Reporting group title	COHORT 3 (NEUROBLASTOMA)
Reporting group description: -	
Reporting group title	COHORT 4 (NON HODGKIN LYMPHOMA)
Reporting group description: -	
Reporting group title	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)
Reporting group description: -	
Reporting group title	COHORT 6 (OSTEOSARCOMA)
Reporting group description: -	
Reporting group title	COHORT 7 (RHABDOMYOSARCOMA)
Reporting group description: -	
Reporting group title	COHORT 8 (WILMS TUMOR)
Reporting group description: -	
Reporting group title	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)
Reporting group description: -	
Reporting group title	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)
Reporting group description: OTHER TUMOR TYPES WITHOUT DOCUMENTED PD-L1 EXPRESSION	
Reporting group title	COHORT 11 (RHABDOID TUMOR)
Reporting group description: -	
Reporting group title	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)
Reporting group description: -	

Reporting group values	COHORT 1 (EWING SARCOMA)	COHORT 2 (HODGKIN LYMPHOMA)	COHORT 3 (NEUROBLASTOMA)
Number of subjects	11	9	11
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	3	2	6
Adolescents (12-17 years)	7	7	2
Adults (18-64 years)	1	0	3
From 65-84 years	0	0	0
85 years and over	0	0	0

Age continuous Units: years			
arithmetic mean	13.6	14.2	12.8
standard deviation	± 3.3	± 3.0	± 9.4
Gender categorical Units: Subjects			
Female	5	6	4
Male	6	3	7
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	1	2
Not Hispanic or Latino	7	5	7
Unknown or Not Reported	2	3	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	8	5	5
More than one race	1	0	1
Unknown or Not Reported	2	4	4

Reporting group values	COHORT 4 (NON HODGKIN LYMPHOMA)	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)	COHORT 6 (OSTEOSARCOMA)
Number of subjects	3	10	10
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	2	0
Adolescents (12-17 years)	1	5	5
Adults (18-64 years)	2	3	5
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	19.0	14.5	17.1
standard deviation	± 6.6	± 6.5	± 4.1
Gender categorical Units: Subjects			
Female	0	5	4
Male	3	5	6
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	2

Not Hispanic or Latino	2	5	6
Unknown or Not Reported	0	4	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	2	6	6
More than one race	0	0	0
Unknown or Not Reported	0	4	2

Reporting group values	COHORT 7 (RHABDOMYOSARCOMA)	COHORT 8 (WILMS TUMOR)	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)
Number of subjects	10	10	4
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	5	5	0
Adolescents (12-17 years)	2	4	4
Adults (18-64 years)	3	1	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	13.0	12.6	14.8
standard deviation	± 8.5	± 6.8	± 1.0
Gender categorical Units: Subjects			
Female	4	6	0
Male	6	4	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	1	2
Not Hispanic or Latino	6	6	2
Unknown or Not Reported	1	3	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	1
White	8	5	1
More than one race	0	0	0
Unknown or Not Reported	2	4	1

Reporting group values	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)	COHORT 11 (RHABDOID TUMOR)	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)
Number of subjects	4	2	3
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	1	0
Infants and toddlers (28 days-23 months)	0	1	0
Children (2-11 years)	3	0	3
Adolescents (12-17 years)	1	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	11.3	0.5	7.3
standard deviation	± 0.5	± 0.7	± 4.6
Gender categorical Units: Subjects			
Female	4	1	1
Male	0	1	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	3	2	0
Unknown or Not Reported	1	0	2
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	0
White	2	2	0
More than one race	0	0	0
Unknown or Not Reported	1	0	2

Reporting group values	Total		
Number of subjects	87		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	1		
Infants and toddlers (28 days-23 months)	1		
Children (2-11 years)	29		

Adolescents (12-17 years)	38		
Adults (18-64 years)	18		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	40		
Male	47		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	16		
Not Hispanic or Latino	51		
Unknown or Not Reported	20		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	3		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	6		
White	50		
More than one race	2		
Unknown or Not Reported	26		

Subject analysis sets

Subject analysis set title	Atezolizumab
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects received intravenous (IV) infusion of atezolizumab (maximum 1200 milligrams [mg]) on Day 1 of each 21-day cycle.	
Subject analysis set title	<2 Age (Years)
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects <2 Age (Years)	
Subject analysis set title	2 to <12 Age (Years)
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects 2 to <12 Age (Years)	
Subject analysis set title	12 to <18 Age (Years)
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects 12 to <18 Age (Years)	
Subject analysis set title	>=18 Age (Years)
Subject analysis set type	Safety analysis
Subject analysis set description: Subjects >=18 Age (Years)	
Subject analysis set title	<18 Age (Years)

Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects <18 Age (Years)

Reporting group values	Atezolizumab	<2 Age (Years)	2 to <12 Age (Years)
Number of subjects	87	2	29
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	1		
Infants and toddlers (28 days-23 months)	1		
Children (2-11 years)	29		
Adolescents (12-17 years)	38		
Adults (18-64 years)	18		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	13.5		
standard deviation	± 6.4	±	±
Gender categorical Units: Subjects			
Female	40		
Male	47		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	16		
Not Hispanic or Latino	51		
Unknown or Not Reported	20		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	3		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	6		
White	50		
More than one race	2		
Unknown or Not Reported	26		

Reporting group values	12 to <18 Age (Years)	>=18 Age (Years)	<18 Age (Years)
Number of subjects	38	18	69
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Gender categorical Units: Subjects			
Female Male			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

End points

End points reporting groups

Reporting group title	COHORT 1 (EWING SARCOMA)
Reporting group description: -	
Reporting group title	COHORT 2 (HODGKIN LYMPHOMA)
Reporting group description: -	
Reporting group title	COHORT 3 (NEUROBLASTOMA)
Reporting group description: -	
Reporting group title	COHORT 4 (NON HODGKIN LYMPHOMA)
Reporting group description: -	
Reporting group title	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)
Reporting group description: -	
Reporting group title	COHORT 6 (OSTEOSARCOMA)
Reporting group description: -	
Reporting group title	COHORT 7 (RHABDOMYOSARCOMA)
Reporting group description: -	
Reporting group title	COHORT 8 (WILMS TUMOR)
Reporting group description: -	
Reporting group title	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)
Reporting group description: -	
Reporting group title	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)
Reporting group description:	
OTHER TUMOR TYPES WITHOUT DOCUMENTED PD-L1 EXPRESSION	
Reporting group title	COHORT 11 (RHABDOID TUMOR)
Reporting group description: -	
Reporting group title	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)
Reporting group description: -	
Subject analysis set title	Atezolizumab
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received intravenous (IV) infusion of atezolizumab (maximum 1200 milligrams [mg]) on Day 1 of each 21-day cycle.	
Subject analysis set title	<2 Age (Years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects <2 Age (Years)	
Subject analysis set title	2 to <12 Age (Years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects 2 to <12 Age (Years)	
Subject analysis set title	12 to <18 Age (Years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects 12 to <18 Age (Years)	
Subject analysis set title	>=18 Age (Years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects >=18 Age (Years)	

Subject analysis set title	<18 Age (Years)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects <18 Age (Years)	

Primary: Percentage of Participants With an Objective Response (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) in Participants With Solid Tumors

End point title	Percentage of Participants With an Objective Response (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) in Participants With Solid Tumors[1][2]

End point description:

Note: In Cohort 5, the response was observed in a rhabdoid tumor. Participant was erroneously enrolled in the Non-rhabdomyosarcoma soft tissue sarcoma cohort.

End point type	Primary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 1 (EWING SARCOMA)	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)	COHORT 6 (OSTEOSARCOMA)	COHORT 7 (RHABDOMYOSARCOMA)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	10
Units: Percentage				
number (not applicable)	0	10	0	0

End point values	COHORT 8 (WILMS TUMOR)	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)	COHORT 11 (RHABDOID TUMOR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	4	4	2
Units: Percentage				
number (not applicable)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Modified International Neuroblastoma Response Criteria (mINRC) in Participants With Neuroblastoma

End point title	Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Modified International Neuroblastoma Response Criteria (mINRC) in Participants With Neuroblastoma[3][4]

End point description:

End point type	Primary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 3 (NEUROBLASTOMA)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Percentage	0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Revised Response Criteria for Malignant Lymphoma for Participants With Hodgkin’s Lymphoma or Non-Hodgkin’s Lymphoma

End point title	Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Revised Response Criteria for Malignant Lymphoma for Participants With Hodgkin’s Lymphoma or Non-Hodgkin’s Lymphoma[5][6]

End point description:

End point type	Primary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 2 (HODGKIN LYMPHOMA)	COHORT 4 (NON HODGKIN LYMPHOMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3		
Units: Percentage				
number (not applicable)	22.2	33.3		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Response Assessment in Neuro-Oncology (RANO) Criteria in Participants With Atypical Teratoid Rhabdoid Tumor (ATRT)

End point title	Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Response Assessment in Neuro-Oncology (RANO) Criteria in Participants With Atypical Teratoid Rhabdoid Tumor (ATRT)[7][8]

End point description:

End point type	Primary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Percentage	0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Clinical Benefit as Determined by the Investigator According to RECIST v1.1 Criteria in Participants With Osteosarcoma

End point title	Percentage of Participants With Clinical Benefit as Determined by the Investigator According to RECIST v1.1 Criteria in Participants With Osteosarcoma[9][10]

End point description:

Included safety-evaluable population (defined as patients who received any amount of study drug), in the Osteosarcoma cohort as per protocol. (Objective response for the other cohorts are measured with different response criteria, and these are described in Outcome Measures 1, 2, 3, and 4).

End point type	Primary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 6 (OSTEOSARCOMA)			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: Percentage	0			

Statistical analyses

No statistical analyses for this end point

Primary: Progression-Free Survival (PFS) as Determined by the Investigator Using RECIST v1.1 in Participants With Solid Tumors

End point title	Progression-Free Survival (PFS) as Determined by the Investigator Using RECIST v1.1 in Participants With Solid Tumors[11][12]

End point description:

End point type	Primary

End point timeframe:

Baseline until first documented occurrence of progressive disease, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 1 (EWING SARCOMA)	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)	COHORT 6 (OSTEOSARCOMA)	COHORT 7 (RHABDOMYOSARCOMA)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	10	10	10
Units: Months				
median (confidence interval 95%)	1.2 (0.6 to 1.4)	1.3 (1.1 to 1.4)	1.2 (0.7 to 1.8)	1.1 (0.8 to 1.3)

End point values	COHORT 8 (WILMS TUMOR)	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)	COHORT 11 (RHABDOID TUMOR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	4	4	2
Units: Months				
median (confidence interval 95%)	1.3 (1.1 to 1.5)	1.2 (0.7 to 1.3)	1.2 (1.1 to 10.1)	0.7 (0.3 to 1.1)

Statistical analyses

No statistical analyses for this end point

Primary: PFS as Determined by the Investigator Using mINRC in Participants With Neuroblastoma

End point title	PFS as Determined by the Investigator Using mINRC in Participants With Neuroblastoma[13][14]

End point description:

End point type	Primary

End point timeframe:

Baseline until first documented occurrence of progressive disease, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 3 (NEUROBLASTOMA)			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Months				
median (confidence interval 95%)	2.6 (1.2 to 4.7)			

Statistical analyses

No statistical analyses for this end point

Primary: PFS as Determined by the Investigator Using Revised Response Criteria for Malignant Lymphoma for Participants With Hodgkin's Lymphoma or Non-Hodgkin's Lymphoma

End point title	PFS as Determined by the Investigator Using Revised Response Criteria for Malignant Lymphoma for Participants With Hodgkin's Lymphoma or Non-Hodgkin's Lymphoma[15][16]

End point description:

End point type	Primary

End point timeframe:

Baseline until first documented occurrence of progressive disease, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 2 (HODGKIN LYMPHOMA)	COHORT 4 (NON HODGKIN LYMPHOMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	3[17]		
Units: Months				
median (confidence interval 95%)	2.8 (2.6 to 4.4)	1.4 (1.1 to 999999)		

Notes:

[17] - Note: 999999=Not estimable. More than 50% patient was censored.

Statistical analyses

No statistical analyses for this end point

Primary: PFS as Determined by the Investigator Using RANO Criteria in Participants With ATRT

End point title	PFS as Determined by the Investigator Using RANO Criteria in Participants With ATRT[18][19]

End point description:

End point type	Primary

End point timeframe:

Baseline until first documented occurrence of progressive disease, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[18] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Months				
median (confidence interval 95%)	1.4 (1.4 to 1.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Adverse Events, Serious Adverse Events and Adverse Events of Special Interest

End point title	Percentage of Participants Adverse Events, Serious Adverse Events and Adverse Events of Special Interest[20]

End point description:

End point type	Primary

End point timeframe:

From baseline up to approximately 42 months

Notes:

[20] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

End point values	Atezolizumab			
Subject group type	Subject analysis set			
Number of subjects analysed	87			
Units: Percentage				
number (not applicable)				
Adverse Events	97.7			
Serious Adverse Events	37.9			
Adverse Events of Special Interest	44.8			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Serum Concentration (Cmax) of Atezolizumab

End point title	Maximum Serum Concentration (Cmax) of Atezolizumab[21]

End point description:

Note: 999999=not available.

End point type	Primary

End point timeframe:

Predose (PRD; 0 hours [hr]), 0.5 hr post-infusion (P-I; infusion duration=30-60 minutes) on Day (D) 1 of Cycle (Cy) 1 and 4 (1 Cy=21 days)

Notes:

[21] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

End point values	<2 Age (Years)	2 to <12 Age (Years)	12 to <18 Age (Years)	>=18 Age (Years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2[22]	26[23]	34[24]	18[25]
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1	105 (± 6.90)	312 (± 28.7)	337 (± 26.8)	424 (± 26.9)
Cycle 4	999999 (± 999999)	382 (± 16.4)	373 (± 78.9)	626 (± 29.2)

Notes:

[22] - For cycle 4, number of subjects analyzed is 0.

[23] - For cycle 4, number of subjects analyzed is 11.

[24] - For cycle 4, number of subjects analyzed is 16.

[25] - For cycle 4, number of subjects analyzed is 6.

Statistical analyses

No statistical analyses for this end point

Primary: Minimum Serum Concentration (Cmin) of Atezolizumab

End point title	Minimum Serum Concentration (Cmin) of Atezolizumab[26]

End point description:

Note: 999999=not available.

End point type	Primary

End point timeframe:

PRD (0 hr) on D1 of Cy2,3,4,8, 12, 16 (1 Cy=21 days) and every 8 cycles thereafter; at any time during visit at study drug discontinuation visit, at least 90 days (maximum 150 days) after the last dose of study drug (up to approximately 42 months)

Notes:

[26] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

End point values	<2 Age (Years)	2 to <12 Age (Years)	12 to <18 Age (Years)	>=18 Age (Years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	1[27]	25[28]	32[29]	16[30]
Units: ug/mL				
geometric mean (geometric coefficient of variation)				
Cycle 2	24.1 (± 999999)	59.3 (± 31.4)	56.5 (± 50.4)	79.9 (± 52.7)
Cycle 3	999999 (± 999999)	58.9 (± 234.4)	85.0 (± 47.4)	148 (± 48.9)
Cycle 4	999999 (± 999999)	99.2 (± 36.4)	113 (± 41.1)	121 (± 80.4)
Cycle 8	999999 (± 999999)	166 (± 19.8)	145 (± 21.9)	209 (± 8.10)

Notes:

[27] - Cycles 3, 4, and 5, number analyzed is 0.

[28] - Cycle(C) 2, number(N) analyzed 25. C3, N analyzed is 13. C4, N analyzed 11. C8, N analyzed 4.

[29] - Cycle(C) 2, number(N) analyzed 32. C3, N analyzed 19. C4, N analyzed 6. C8, N analyzed 4.

[30] - Cycle(C) 2, number(N) analyzed 16. C3, N analyzed 8. C4, N analyzed 6. C8, N analyzed 2.

Statistical analyses

No statistical analyses for this end point

Primary: Atezolizumab Serum Concentration at Washout

End point title	Atezolizumab Serum Concentration at Washout[31]

End point description:

End point type	Primary

End point timeframe:

At least 90 days (maximum 150 days) after last dose of study drug (up to approximately 42 months)

Notes:

[31] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

End point values	Atezolizumab			
Subject group type	Subject analysis set			
Number of subjects analysed	17			
Units: ug/mL				
geometric mean (geometric coefficient of variation)	1.91 (± 2815.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve (AUC) of Atezolizumab

End point title	Area Under the Concentration-Time Curve (AUC) of Atezolizumab[32]

End point description:

End point type	Primary

End point timeframe:

D1 of Cy1 (1 Cy=21 days)

Notes:

[32] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

End point values	<2 Age (Years)	2 to <12 Age (Years)	12 to <18 Age (Years)	>=18 Age (Years)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	2	29	38	18
Units: ugxday/mL				
geometric mean (geometric coefficient of variation)	1130 (± 5.28)	2209 (± 21.3)	2816 (± 17.7)	3579 (± 28.4)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Anti-Therapeutic Antibodies (ATAs) to Atezolizumab

End point title	Percentage of Participants With Anti-Therapeutic Antibodies (ATAs) to Atezolizumab[33]

End point description:

End point type	Primary

End point timeframe:

PRD (0 hr) on D1 of Cy1,2,3,4,8,12,16 (1 Cy=21 days) & every 8 cycles thereafter; at any time during visit on Cy1D8, study drug discontinuation, at least 90 days (maximum 150 days) after last dose of study drug (up to approximately 42 months)

Notes:

[33] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis for this end point.

End point values	Atezolizumab			
Subject group type	Subject analysis set			
Number of subjects analysed	78			
Units: Percentage				
number (not applicable)				
Baseline	2.6			
Post-baseline	14.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as Determined by the Investigator Using RECIST v1.1 Criteria in Participants With Solid Tumors

End point title	Duration of Response (DOR) as Determined by the Investigator Using RECIST v1.1 Criteria in Participants With Solid Tumors[34]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 1 (EWING SARCOMA)	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)	COHORT 6 (OSTEOSARCOMA)	COHORT 7 (RHABDOMYOSARCOMA)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[35]	1[36]	0[37]	0[38]
Units: Months				
median (confidence interval 95%)	(to)	13.2 (000000 to 999999)	(to)	(to)

Notes:

[35] - There was no objective response.

[36] - Note: 000000=not estimable. 9999999= not estimable. There was only 1 participant.

[37] - There was no objective response.

[38] - There was no objective response.

End point values	COHORT 8 (WILMS TUMOR)	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)	COHORT 11 (RHABDOID TUMOR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[39]	0[40]	0[41]	0[42]
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[39] - There was no objective response.

[40] - There was no objective response.

[41] - There was no objective response.

[42] - There was no objective response.

Statistical analyses

No statistical analyses for this end point

Secondary: DOR as Determined by the Investigator Using mINRC in Participants With Neuroblastoma

End point title	DOR as Determined by the Investigator Using mINRC in Participants With Neuroblastoma[43]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 3 (NEUROBLASTOMA)			
Subject group type	Reporting group			
Number of subjects analysed	0[44]			
Units: Months				
median (confidence interval 95%)	(to)			

Notes:

[44] - No subjects had an objective response.

Statistical analyses

No statistical analyses for this end point

Secondary: DOR as Determined by the Investigator Using Revised Response Criteria for Malignant Lymphoma for Participants With Hodgkin’s Lymphoma or Non-Hodgkin’s Lymphoma

End point title	DOR as Determined by the Investigator Using Revised Response Criteria for Malignant Lymphoma for Participants With Hodgkin’s Lymphoma or Non-Hodgkin’s Lymphoma[45]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 2 (HODGKIN LYMPHOMA)	COHORT 4 (NON HODGKIN LYMPHOMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2[46]	1[47]		
Units: Months				
median (confidence interval 95%)	999999 (4.1 to 999999)	999999 (999999 to 999999)		

Notes:

[46] - Note: 999999= not estimable. Kaplan-Meier median estimate not reached.

[47] - Note: 999999= not estimable. Kaplan-Meier median estimate not reached.

Statistical analyses

No statistical analyses for this end point

Secondary: DOR as Determined by the Investigator Using RANO Criteria in Participants With ATRT

End point title	DOR as Determined by the Investigator Using RANO Criteria in Participants With ATRT[48]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)			
Subject group type	Reporting group			
Number of subjects analysed	0[49]			
Units: Months				
median (confidence interval 95%)	(to)			

Notes:

[49] - No subjects had an objective response.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

End point type	Secondary

End point timeframe:

Baseline until death (up to approximately 42 months)

End point values	Atezolizumab			
Subject group type	Subject analysis set			
Number of subjects analysed	87			
Units: Months				
median (confidence interval 95%)	7.4 (5.3 to 9.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Immune-Modified RECIST v1.1 for Participants With Other Solid Tumors

End point title	Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Immune-Modified RECIST v1.1 for Participants With Other Solid Tumors[50]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 1 (EWING SARCOMA)	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)	COHORT 6 (OSTEOSARCOMA)	COHORT 7 (RHABDOMYOSARCOMA)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[51]	0[52]	0[53]	0[54]
Units: Percentage				

Notes:

[51] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[52] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[53] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[54] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

End point values	COHORT 8 (WILMS TUMOR)	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)	COHORT 11 (RHABDOID TUMOR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[55]	0[56]	0[57]	0[58]
Units: Percentage				

Notes:

[55] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[56] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[57] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[58] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

End point values	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)			
Subject group type	Reporting group			
Number of subjects analysed	0[59]			
Units: Percentage				

Notes:

[59] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using irRC for Participants With Hodgkin's Lymphoma or Non-Hodgkin's Lymphoma

End point title	Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using irRC for Participants With Hodgkin's Lymphoma or Non-Hodgkin's Lymphoma[60]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[60] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this end point.

End point values	COHORT 2 (HODGKIN LYMPHOMA)	COHORT 4 (NON HODGKIN LYMPHOMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[61]	0[62]		
Units: Percentage				

Notes:

[61] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[62] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Immune-Related Response Criteria (irRC) for Participants With Neuroblastoma

End point title	Percentage of Participants With an Objective Response (CR or PR) as Determined by the Investigator Using Immune-Related Response Criteria (irRC) for Participants With Neuroblastoma[63]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[63] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 3 (NEUROBLASTOMA)			
Subject group type	Reporting group			
Number of subjects analysed	0[64]			
Units: Percentage				

Notes:

[64] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Determined by the Investigator Using Immune-Modified RECIST v1.1 for Participants With Other Solid Tumors

End point title	PFS as Determined by the Investigator Using Immune-Modified RECIST v1.1 for Participants With Other Solid Tumors[65]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately

42 months)

Notes:

[65] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this end point.

End point values	COHORT 1 (EWING SARCOMA)	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)	COHORT 6 (OSTEOSARCOMA)	COHORT 7 (RHABDOMYOSARCOMA)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[66]	0[67]	0[68]	0[69]
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[66] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[67] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[68] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[69] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

End point values	COHORT 8 (WILMS TUMOR)	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)	COHORT 11 (RHABDOID TUMOR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[70]	0[71]	0[72]	0[73]
Units: Months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[70] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[71] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[72] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[73] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

End point values	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)			
Subject group type	Reporting group			
Number of subjects analysed	0[74]			
Units: Months				
median (confidence interval 95%)	(to)			

Notes:

[74] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Determined by the Investigator Using irRC for Participants With Hodgkin's Lymphoma or Non-Hodgkin's Lymphoma

End point title	PFS as Determined by the Investigator Using irRC for Participants With Hodgkin's Lymphoma or Non-Hodgkin's Lymphoma[75]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 2 (HODGKIN LYMPHOMA)	COHORT 4 (NON HODGKIN LYMPHOMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[76]	0[77]		
Units: Months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[76] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[77] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: PFS as Determined by the Investigator Using irRC for Participants With Neuroblastoma

End point title	PFS as Determined by the Investigator Using irRC for Participants With Neuroblastoma[78]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[78] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 3 (NEUROBLASTOMA)			
Subject group type	Reporting group			
Number of subjects analysed	0[79]			
Units: Months				
median (confidence interval 95%)	(to)			

Notes:

[79] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: DOR as Determined by the Investigator Using Immune-Modified RECIST v1.1 for Participants With Other Solid Tumors

End point title	DOR as Determined by the Investigator Using Immune-Modified RECIST v1.1 for Participants With Other Solid Tumors[80]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[80] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 1 (EWING SARCOMA)	COHORT 5 (NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA)	COHORT 6 (OSTEOSARCOMA)	COHORT 7 (RHABDOMYOSARCOMA)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[81]	0[82]	0[83]	0[84]
Units: Months				

Notes:

[81] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[82] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[83] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[84] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

End point values	COHORT 8 (WILMS TUMOR)	COHORT 9 (OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION)	COHORT 10 (OTHER TUMOR TYPES WITHOUT PD-L1 EXPRESSION)	COHORT 11 (RHABDOID TUMOR)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[85]	0[86]	0[87]	0[88]
Units: Months				

Notes:

[85] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[86] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[87] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[88] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

End point values	COHORT 12 (ATYPICAL TERATOID RHABDOID TUMOR)			
Subject group type	Reporting group			
Number of subjects analysed	0[89]			
Units: Months				

Notes:

[89] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: DOR as Determined by the Investigator Using irRC for Participants With Neuroblastoma

End point title	DOR as Determined by the Investigator Using irRC for Participants With Neuroblastoma[90]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[90] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 3 (NEUROBLASTOMA)			
Subject group type	Reporting group			
Number of subjects analysed	0[91]			
Units: Percentage				
median (confidence interval 95%)	(to)			

Notes:

[91] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: DOR as Determined by the Investigator Using irRC for Participants With Hodgkin’s Lymphoma or Non-Hodgkin’s Lymphoma

End point title	DOR as Determined by the Investigator Using irRC for Participants With Hodgkin’s Lymphoma or Non-Hodgkin’s Lymphoma[92]

End point description:

End point type	Secondary

End point timeframe:

Baseline until disease progression, or death from any cause, whichever occurs first (up to approximately 42 months)

Notes:

[92] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	COHORT 2 (HODGKIN LYMPHOMA)	COHORT 4 (NON HODGKIN LYMPHOMA)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[93]	0[94]		
Units: Months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[93] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

[94] - Analysis not conducted due to limited objective responses using primary evaluation criteria.

Statistical analyses

No statistical analyses for this end point

Secondary: Optimal Dose of Atezolizumab in Pediatric Participants

End point title	Optimal Dose of Atezolizumab in Pediatric Participants

End point description:

Atezolizumab was administered on Day 1 only for a cycle duration of 3 weeks.

End point type	Secondary

End point timeframe:

From baseline up to approximately 42 months

End point values	<18 Age (Years)			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: mg/kg				
<18 Age (Years)	15			

Statistical analyses

No statistical analyses for this end point

Secondary: Optimal Dose of Atezolizumab in Young Adult Participants

End point title	Optimal Dose of Atezolizumab in Young Adult Participants

End point description:

Atezolizumab was administered on Day 1 only for a cycle duration of 3 weeks.

End point type	Secondary

End point timeframe:

From baseline up to approximately 42 months

End point values	>=18 Age (Years)			
Subject group type	Subject analysis set			
Number of subjects analysed	18			
Units: mg	1200			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to approximately 42 months

Adverse event reporting additional description:

Adverse Events reporting is for the Safety Evaluable Population, defined as patients who received any amount of any component of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	COHORT 1

Reporting group description:

EWING SARCOMA

Reporting group title	COHORT 2

Reporting group description:

HODGKIN LYMPHOMA

Reporting group title	COHORT 5

Reporting group description:

NON-RHABDOMYOSARCOMA SOFT TISSUE SARCOMA;

Reporting group title	COHORT 4

Reporting group description:

NON HODGKIN LYMPHOMA

Reporting group title	COHORT 3

Reporting group description:

NEUROBLASTOMA

Reporting group title	COHORT 6

Reporting group description:

OSTEOSARCOMA

Reporting group title	COHORT 7

Reporting group description:

RHABDOMYOSARCOMA

Reporting group title	COHORT 8

Reporting group description:

WILMS TUMOR

Reporting group title	COHORT 9

Reporting group description:

OTHER TUMOR TYPES WITH DOCUMENTED PD-L1 EXPRESSION

Reporting group title	COHORT 10

Reporting group description:

OTHER TUMOR TYPES WITHOUT DOCUMENTED PD-L1 EXPRESSION

Reporting group title	COHORT 11

Reporting group description:

RHABDOID TUMOR

Reporting group title	COHORT 12

Reporting group description:

ATYPICAL TERATOID RHABDOID TUMOR

Serious adverse events	COHORT 1	COHORT 2	COHORT 5
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 11 (36.36%)	3 / 9 (33.33%)	3 / 10 (30.00%)
number of deaths (all causes)	6	5	9
number of deaths resulting from adverse events			
Vascular disorders			
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPERIOR VENA CAVA SYNDROME			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			

GRAFT VERSUS HOST DISEASE			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
POSTOPERATIVE HYPOTENSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXICITY TO VARIOUS AGENTS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
HEADACHE			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDROCEPHALUS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAESTHESIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITH NERVE DISORDER			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
PAPILLOEDEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CONSTIPATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLESTASIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
PRURITUS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXIC SKIN ERUPTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
BONE PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLANK PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCISION SITE ABSCESS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG INFECTION			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE ABSCESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	COHORT 4	COHORT 3	COHORT 6
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	6 / 10 (60.00%)
number of deaths (all causes)	2	7	8
number of deaths resulting from adverse events			
Vascular disorders			
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPERIOR VENA CAVA SYNDROME			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
GRAFT VERSUS HOST DISEASE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
POSTOPERATIVE HYPOTENSION			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXICITY TO VARIOUS AGENTS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDROCEPHALUS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAESTHESIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITH NERVE DISORDER			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

PAPILLOEDEMA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLESTASIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
PRURITUS			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXIC SKIN ERUPTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
BONE PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLANK PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCISION SITE ABSCESS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE ABSCESS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	COHORT 7	COHORT 8	COHORT 9
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	5 / 10 (50.00%)	2 / 4 (50.00%)
number of deaths (all causes)	9	9	3
number of deaths resulting from adverse events			
Vascular disorders			
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPERIOR VENA CAVA SYNDROME			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST PAIN			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
GRAFT VERSUS HOST DISEASE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
POSTOPERATIVE HYPOTENSION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXICITY TO VARIOUS AGENTS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDROCEPHALUS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAESTHESIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VITH NERVE DISORDER			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
PAPILLOEDEMA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hepatobiliary disorders			
CHOLESTASIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
PRURITUS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXIC SKIN ERUPTION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
BONE PAIN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLANK PAIN			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCISION SITE ABSCESS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE ABSCESS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	COHORT 10	COHORT 11	COHORT 12
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
number of deaths (all causes)	4	2	3
number of deaths resulting from adverse events			
Vascular disorders			
SHOCK HAEMORRHAGIC			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

SUPERIOR VENA CAVA SYNDROME			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
CHEST PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
GRAFT VERSUS HOST DISEASE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
POSTOPERATIVE HYPOTENSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXICITY TO VARIOUS AGENTS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
HEADACHE			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYDROCEPHALUS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAESTHESIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

VITH NERVE DISORDER			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
PAPILLOEDEMA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLESTASIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
PRURITUS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXIC SKIN ERUPTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
BONE PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLANK PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL ABSCESS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INCISION SITE ABSCESS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE ABSCESS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPTIC SHOCK			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	COHORT 1	COHORT 2	COHORT 5
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)	8 / 9 (88.89%)	10 / 10 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR INFLAMMATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
TUMOUR PAIN			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HOT FLUSH			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HYPERTENSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
HYPOTENSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPOVOLAEMIC SHOCK			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VENOUS THROMBOSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Surgical and medical procedures			
CENTRAL VENOUS CATHETERISATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

ASTHENIA			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
AXILLARY PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CATHETER SITE ERYTHEMA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
CHEST DISCOMFORT			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CHEST PAIN			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
CHILLS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
FACE OEDEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	2 / 11 (18.18%)	2 / 9 (22.22%)	4 / 10 (40.00%)
occurrences (all)	3	2	13
GENERALISED OEDEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
MALAISE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

OEDEMA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PAIN			
subjects affected / exposed	2 / 11 (18.18%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	2	1	2
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
PYREXIA			
subjects affected / exposed	3 / 11 (27.27%)	3 / 9 (33.33%)	2 / 10 (20.00%)
occurrences (all)	5	9	5
THIRST			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
VACCINATION SITE OEDEMA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
PELVIC PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VAGINAL DISCHARGE			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
CATARRH			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
COUGH			

subjects affected / exposed	3 / 11 (27.27%)	4 / 9 (44.44%)	1 / 10 (10.00%)
occurrences (all)	4	14	1
DYSPHONIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
HYPOXIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
IRREGULAR BREATHING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
LARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
DISORDER OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PHARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PNEUMONITIS			

subjects affected / exposed	0 / 11 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
STRIDOR			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
TACHYPNOEA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ATELECTASIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
RHINORRHOEA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
ANXIETY			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
BRUXISM			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

DELIRIUM			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
INSOMNIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
IRRITABILITY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	4
SLEEP DISORDER			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
ABNORMAL BEHAVIOUR			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Product issues			
DEVICE BREAKAGE			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	3	1
AMYLASE INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
ANTITHROMBIN III DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
BLOOD ALKALINE PHOSPHATASE			

INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BLOOD CHLORIDE DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	2 / 11 (18.18%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BLOOD POTASSIUM DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BLOOD THYROID STIMULATING HORMONE INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
BLOOD URINE PRESENT			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
CANDIDA TEST POSITIVE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CARDIAC MURMUR			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LIPASE INCREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	4
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	4
NOROVIRUS TEST POSITIVE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OXYGEN SATURATION DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	3
PROTHROMBIN LEVEL DECREASED			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
VITAMIN K DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
WEIGHT DECREASED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
WHITE BLOOD CELL COUNT DECREASED			

subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	2	0	3
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	1	2
LIMB INJURY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
POST PROCEDURAL SWELLING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PROCEDURAL PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
THERMAL BURN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
UROSTOMY COMPLICATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
WOUND DEHISCENCE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
CONTUSION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
FANCONI SYNDROME			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			

PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SINUS TACHYCARDIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
TACHYCARDIA			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
Nervous system disorders			
AMPUTATION STUMP PAIN			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DYSGEUSIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
HEADACHE			
subjects affected / exposed	2 / 11 (18.18%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	2	8	3
HYPOAESTHESIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
MIGRAINE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
MIGRAINE WITH AURA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
NEURALGIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
PARAESTHESIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
PHANTOM LIMB SYNDROME			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SEIZURE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SOMNOLENCE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
TREMOR			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
DIZZINESS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PARAPARESIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	3 / 11 (27.27%)	1 / 9 (11.11%)	5 / 10 (50.00%)
occurrences (all)	4	1	12
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LEUKOPENIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LYMPHADENOPATHY			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	2
LYMPHOPENIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	2
NEUTROPENIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1

THROMBOCYTOPENIA			
subjects affected / exposed	2 / 11 (18.18%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	3	2	0
THROMBOCYTOSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	1 / 11 (9.09%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	1	3	0
VERTIGO			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
ECZEMA EYELIDS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
EYELID PTOSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OPSOCLONUS MYOCLONUS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PERIORBITAL OEDEMA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PHOTOPHOBIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
PHOTOPSIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

ABDOMINAL PAIN			
subjects affected / exposed	3 / 11 (27.27%)	2 / 9 (22.22%)	2 / 10 (20.00%)
occurrences (all)	3	2	4
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
ANAL INCONTINENCE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ASCITES			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
COLITIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
CONSTIPATION			
subjects affected / exposed	3 / 11 (27.27%)	1 / 9 (11.11%)	6 / 10 (60.00%)
occurrences (all)	6	1	6
DENTAL CARIES			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
DIARRHOEA			
subjects affected / exposed	0 / 11 (0.00%)	2 / 9 (22.22%)	4 / 10 (40.00%)
occurrences (all)	0	3	6
DYSPEPSIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
ENTEROCOLITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

HAEMATOCHEZIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LIP ULCERATION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	4 / 11 (36.36%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	4	3	2
NONINFECTIVE GINGIVITIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
ODYNOPHAGIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
ORAL PAIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PROCTALGIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
RECTAL DISCHARGE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
SUBILEUS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SWOLLEN TONGUE			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
UPPER GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
VOMITING			
subjects affected / exposed	3 / 11 (27.27%)	3 / 9 (33.33%)	3 / 10 (30.00%)
occurrences (all)	4	6	5
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
BLISTER			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DERMATITIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
DERMATITIS CONTACT			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
DRY SKIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
ECZEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ERYTHEMA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
HYPERHIDROSIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PALMAR-PLANTAR			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
PERIORAL DERMATITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PETECHIAE			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PITYRIASIS ROSEA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
PRURITUS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
RASH			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
RASH PRURITIC			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
URTICARIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

DYSURIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
GLYCOSURIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HAEMATURIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYDRONEPHROSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OLIGURIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PROTEINURIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
URINARY INCONTINENCE			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
URINARY RETENTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	0 / 11 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	3	0
HYPOTHYROIDISM			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			

ARTHRALGIA			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
BACK PAIN			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
FLANK PAIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
HAEMARTHROSIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	0	1	2
MYALGIA			
subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
NECK PAIN			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
PAIN IN EXTREMITY			
subjects affected / exposed	2 / 11 (18.18%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	4	2	2
PAIN IN JAW			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
JOINT SWELLING			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
BACTERAEMIA			

subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
BRONCHITIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
CANDIDA URETHRITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
DERMATOPHYTOSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
FUNGAL SKIN INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
GENITAL HERPES			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HERPES VIRUS INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
INFLUENZA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
LARYNGITIS			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
LUNG INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			

subjects affected / exposed	1 / 11 (9.09%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
ORAL HERPES			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PARONYCHIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PHARYNGITIS			
subjects affected / exposed	0 / 11 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
PYELONEPHRITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	0 / 11 (0.00%)	4 / 9 (44.44%)	1 / 10 (10.00%)
occurrences (all)	0	16	1
SKIN INFECTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
STAPHYLOCOCCAL			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
TONSILLITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

VASCULAR DEVICE INFECTION			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
VULVITIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	4 / 11 (36.36%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	4	1	4
DEHYDRATION			
subjects affected / exposed	2 / 11 (18.18%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPERKALAEMIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
HYPERNATRAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPERURICAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPOCALCAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPOKALAEMIA			

subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPONATRAEMIA			
subjects affected / exposed	1 / 11 (9.09%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPERMAGNESAEMIA			
subjects affected / exposed	0 / 11 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	COHORT 4	COHORT 3	COHORT 6
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	11 / 11 (100.00%)	10 / 10 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR INFLAMMATION			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
TUMOUR PAIN			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HOT FLUSH			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			

subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
HYPOTENSION			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HYPOVOLAEMIC SHOCK			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VENOUS THROMBOSIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
CENTRAL VENOUS CATHETERISATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
AXILLARY PAIN			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
CATHETER SITE ERYTHEMA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CHEST DISCOMFORT			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
CHEST PAIN			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	0	1	5
CHILLS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
FACE OEDEMA			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
FATIGUE			
subjects affected / exposed	0 / 3 (0.00%)	3 / 11 (27.27%)	6 / 10 (60.00%)
occurrences (all)	0	3	6
GENERALISED OEDEMA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	2	2
MALAISE			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OEDEMA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	2 / 3 (66.67%)	4 / 11 (36.36%)	8 / 10 (80.00%)
occurrences (all)	2	5	14
THIRST			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VACCINATION SITE OEDEMA			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
PELVIC PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VAGINAL DISCHARGE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
CATARRH			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	1 / 3 (33.33%)	2 / 11 (18.18%)	5 / 10 (50.00%)
occurrences (all)	1	2	8
DYSPHONIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
DYSPNOEA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
EPISTAXIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPOXIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
IRREGULAR BREATHING			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
NASAL CONGESTION			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	0	2	2
DISORDER OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PHARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PLEURAL EFFUSION			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
PNEUMONITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
STRIDOR			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
TACHYPNOEA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
ATELECTASIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ANXIETY			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
BRUXISM			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
DELIRIUM			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
DEPRESSION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
IRRITABILITY			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SLEEP DISORDER			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ABNORMAL BEHAVIOUR			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0

Product issues			
DEVICE BREAKAGE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	3 / 11 (27.27%)	2 / 10 (20.00%)
occurrences (all)	0	3	3
AMYLASE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ANTITHROMBIN III DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	4 / 11 (36.36%)	2 / 10 (20.00%)
occurrences (all)	0	4	2
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
BLOOD CHLORIDE DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
BLOOD POTASSIUM DECREASED			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BLOOD THYROID STIMULATING HORMONE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BLOOD URINE PRESENT			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CANDIDA TEST POSITIVE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CARDIAC MURMUR			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
LIPASE INCREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	3 / 10 (30.00%)
occurrences (all)	0	1	6
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
NOROVIRUS TEST POSITIVE			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OXYGEN SATURATION DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
PROTHROMBIN LEVEL DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VITAMIN K DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 3 (33.33%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	1	1	1
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	0	2	4
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
FALL			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LIMB INJURY			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
POST PROCEDURAL SWELLING			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PROCEDURAL PAIN			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
THERMAL BURN			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
UROSTOMY COMPLICATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
WOUND DEHISCENCE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CONTUSION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
FANCONI SYNDROME			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
TACHYCARDIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Nervous system disorders			
AMPUTATION STUMP PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
DYSGEUSIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
HEADACHE			

subjects affected / exposed	1 / 3 (33.33%)	3 / 11 (27.27%)	2 / 10 (20.00%)
occurrences (all)	1	3	8
HYPOAESTHESIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
MIGRAINE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
MIGRAINE WITH AURA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
NEURALGIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
PHANTOM LIMB SYNDROME			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
SEIZURE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SOMNOLENCE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
TREMOR			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DIZZINESS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
PARAPARESIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			

ANAEMIA			
subjects affected / exposed	1 / 3 (33.33%)	3 / 11 (27.27%)	2 / 10 (20.00%)
occurrences (all)	1	6	2
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LEUKOPENIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LYMPHADENOPATHY			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LYMPHOPENIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
THROMBOCYTOSIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VERTIGO			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Eye disorders			
ECZEMA EYELIDS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
EYELID PTOSIS			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OPSOCLONUS MYOCLONUS			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PERIORBITAL OEDEMA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PHOTOPHOBIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PHOTOPSIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
VISION BLURRED			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	3 / 10 (30.00%)
occurrences (all)	0	2	3
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ANAL INCONTINENCE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ASCITES			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
COLITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

CONSTIPATION			
subjects affected / exposed	1 / 3 (33.33%)	2 / 11 (18.18%)	6 / 10 (60.00%)
occurrences (all)	1	2	7
DENTAL CARIES			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
DIARRHOEA			
subjects affected / exposed	0 / 3 (0.00%)	4 / 11 (36.36%)	4 / 10 (40.00%)
occurrences (all)	0	5	5
DYSPEPSIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
DYSPHAGIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ENTEROCOLITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HAEMATOCHEZIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
LIP ULCERATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	4 / 10 (40.00%)
occurrences (all)	0	2	7
NONINFECTIVE GINGIVITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ODYNOPHAGIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ORAL PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

PROCTALGIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
RECTAL DISCHARGE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
SUBILEUS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SWOLLEN TONGUE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	3 / 10 (30.00%)
occurrences (all)	0	2	4
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BLISTER			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DERMATITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DRY SKIN			
subjects affected / exposed	1 / 3 (33.33%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
ECZEMA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ERYTHEMA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	3
PALMAR-PLANTAR			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
PERIORAL DERMATITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PETECHIAE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PITYRIASIS ROSEA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
RASH			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
RASH MACULO-PAPULAR			

subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
RASH PRURITIC			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
URTICARIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
DYSURIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
GLYCOSURIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
HAEMATURIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HYDRONEPHROSIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
OLIGURIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PROTEINURIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2

URINARY INCONTINENCE			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
URINARY RETENTION			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPOTHYROIDISM			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
BACK PAIN			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	0	3	4
FLANK PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HAEMARTHROSIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
MYALGIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
NECK PAIN			

subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	0	2	3
PAIN IN JAW			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
JOINT SWELLING			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
BACTERAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
BRONCHITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CANDIDA URETHRITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
DERMATOPHYTOSIS			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
FUNGAL SKIN INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
GENITAL HERPES			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

HERPES VIRUS INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
LARYNGITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
LUNG INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
ORAL HERPES			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
PARONYCHIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	1 / 3 (33.33%)	0 / 11 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
PYELONEPHRITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	1 / 3 (33.33%)	2 / 11 (18.18%)	1 / 10 (10.00%)
occurrences (all)	1	2	2
SKIN INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

STAPHYLOCOCCAL			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
TONSILLITIS			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VASCULAR DEVICE INFECTION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
VULVITIS			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 3 (0.00%)	2 / 11 (18.18%)	2 / 10 (20.00%)
occurrences (all)	0	2	2
DEHYDRATION			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
HYPERKALAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HYPERNATRAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPERTRIGLYCERIDAEMIA			

subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HYPERURICAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
HYPOCALCAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	0 / 11 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	2 / 10 (20.00%)
occurrences (all)	0	1	3
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
HYPERMAGNESAEMIA			
subjects affected / exposed	0 / 3 (0.00%)	1 / 11 (9.09%)	0 / 10 (0.00%)
occurrences (all)	0	3	0

Non-serious adverse events	COHORT 7	COHORT 8	COHORT 9
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)	10 / 10 (100.00%)	4 / 4 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR INFLAMMATION			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
TUMOUR PAIN			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HOT FLUSH			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
HYPOTENSION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
HYPOVOLAEMIC SHOCK			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
VENOUS THROMBOSIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
CENTRAL VENOUS CATHETERISATION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
AXILLARY PAIN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CATHETER SITE ERYTHEMA			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CHEST DISCOMFORT			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CHEST PAIN			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
CHILLS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
FACE OEDEMA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
FATIGUE			
subjects affected / exposed	3 / 10 (30.00%)	6 / 10 (60.00%)	1 / 4 (25.00%)
occurrences (all)	3	7	1
GENERALISED OEDEMA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
MALAISE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
OEDEMA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
PAIN			

subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	5 / 10 (50.00%)	4 / 10 (40.00%)	1 / 4 (25.00%)
occurrences (all)	6	5	2
THIRST			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
VACCINATION SITE OEDEMA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
PELVIC PAIN			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
VAGINAL DISCHARGE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
CATARRH			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
COUGH			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	2 / 4 (50.00%)
occurrences (all)	0	1	2
DYSPHONIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
DYSPNOEA			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
HYPOXIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
IRREGULAR BREATHING			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
LARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DISORDER OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
PHARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
PNEUMONITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
STRIDOR			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
TACHYPNOEA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
ATELECTASIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ANXIETY			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
BRUXISM			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DELIRIUM			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

INSOMNIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
IRRITABILITY			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
SLEEP DISORDER			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ABNORMAL BEHAVIOUR			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Product issues			
DEVICE BREAKAGE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
AMYLASE INCREASED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
ANTITHROMBIN III DECREASED			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 4 (25.00%)
occurrences (all)	0	4	1
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

BLOOD CHLORIDE DECREASED			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	0 / 4 (0.00%)
occurrences (all)	0	3	0
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
BLOOD POTASSIUM DECREASED			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
BLOOD THYROID STIMULATING HORMONE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
BLOOD URINE PRESENT			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
CANDIDA TEST POSITIVE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
CARDIAC MURMUR			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
LIPASE INCREASED			

subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 4 (25.00%)
occurrences (all)	0	5	1
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	5	0
NOROVIRUS TEST POSITIVE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
OXYGEN SATURATION DECREASED			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 4 (25.00%)
occurrences (all)	0	4	1
PROTHROMBIN LEVEL DECREASED			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
VITAMIN K DECREASED			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences (all)	0	4	1
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
FALL			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
LIMB INJURY			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
POST PROCEDURAL SWELLING			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
PROCEDURAL PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
THERMAL BURN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
UROSTOMY COMPLICATION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
WOUND DEHISCENCE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CONTUSION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
FANCONI SYNDROME			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
TACHYCARDIA			

subjects affected / exposed	2 / 10 (20.00%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences (all)	2	1	1
Nervous system disorders			
AMPUTATION STUMP PAIN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DYSGEUSIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	2 / 10 (20.00%)	3 / 10 (30.00%)	0 / 4 (0.00%)
occurrences (all)	2	5	0
HYPOAESTHESIA			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
MIGRAINE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
MIGRAINE WITH AURA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NEURALGIA			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
PARAESTHESIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PHANTOM LIMB SYNDROME			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
SEIZURE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
SOMNOLENCE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

TREMOR			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DIZZINESS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	2
PARAPARESIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	3 / 10 (30.00%)	2 / 10 (20.00%)	1 / 4 (25.00%)
occurrences (all)	3	2	1
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
LEUKOPENIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
LYMPHADENOPATHY			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
LYMPHOPENIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
NEUTROPENIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
THROMBOCYTOSIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			

EAR PAIN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
VERTIGO			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
ECZEMA EYELIDS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
EYELID PTOSIS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
OPSOCLONUS MYOCLONUS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PERIORBITAL OEDEMA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PHOTOPHOBIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PHOTOPSIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 10 (10.00%)	3 / 10 (30.00%)	0 / 4 (0.00%)
occurrences (all)	1	5	0
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
ABDOMINAL PAIN UPPER			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ANAL INCONTINENCE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
ASCITES			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
COLITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	2 / 10 (20.00%)	6 / 10 (60.00%)	1 / 4 (25.00%)
occurrences (all)	2	7	1
DENTAL CARIES			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DIARRHOEA			
subjects affected / exposed	2 / 10 (20.00%)	2 / 10 (20.00%)	1 / 4 (25.00%)
occurrences (all)	3	2	1
DYSPEPSIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ENTEROCOLITIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
HAEMATOCHEZIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
LIP ULCERATION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NAUSEA			

subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	1 / 4 (25.00%)
occurrences (all)	0	2	2
NONINFECTIVE GINGIVITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ODYNOPHAGIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ORAL PAIN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PROCTALGIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
RECTAL DISCHARGE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
STOMATITIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
SUBILEUS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
SWOLLEN TONGUE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	1 / 10 (10.00%)	4 / 10 (40.00%)	1 / 4 (25.00%)
occurrences (all)	2	5	2
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			

subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
BLISTER			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
DERMATITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DRY SKIN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ECZEMA			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
ERYTHEMA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPERHIDROSIS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
PALMAR-PLANTAR			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PERIORAL DERMATITIS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

PETECHIAE			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PITYRIASIS ROSEA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
RASH			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
RASH PRURITIC			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
URTICARIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
DYSURIA			
subjects affected / exposed	0 / 10 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
GLYCOSURIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HAEMATURIA			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
HYDRONEPHROSIS			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
OLIGURIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
PROTEINURIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
URINARY INCONTINENCE			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
URINARY RETENTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPOTHYROIDISM			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
BACK PAIN			
subjects affected / exposed	1 / 10 (10.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
FLANK PAIN			

subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
HAEMARTHROSIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
NECK PAIN			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
PAIN IN JAW			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
JOINT SWELLING			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
BACTERAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
BRONCHITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
CANDIDA URETHRITIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

CONJUNCTIVITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DERMATOPHYTOSIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
FUNGAL SKIN INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
GENITAL HERPES			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HERPES VIRUS INFECTION			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
INFLUENZA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
LARYNGITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
LUNG INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
ORAL HERPES			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

PARONYCHIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
PYELONEPHRITIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
RHINITIS			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
SKIN INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
STAPHYLOCOCCAL			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
TONSILLITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
VASCULAR DEVICE INFECTION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
VULVITIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

DECREASED APPETITE			
subjects affected / exposed	1 / 10 (10.00%)	4 / 10 (40.00%)	1 / 4 (25.00%)
occurrences (all)	1	5	1
DEHYDRATION			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
HYPERKALAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
HYPERNATRAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPERURICAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPOCALCAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
HYPOKALAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPOMAGNESAEMIA			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	4	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	3 / 10 (30.00%)	1 / 4 (25.00%)
occurrences (all)	0	3	1

HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 10 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
HYPERMAGNESAEMIA			
subjects affected / exposed	1 / 10 (10.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	1	4	0

Non-serious adverse events	COHORT 10	COHORT 11	COHORT 12
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 4 (75.00%)	2 / 2 (100.00%)	2 / 3 (66.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR INFLAMMATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TUMOUR PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
EMBOLISM			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HOT FLUSH			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPOTENSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPOVOLAEMIC SHOCK			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VENOUS THROMBOSIS			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
CENTRAL VENOUS CATHETERISATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
AXILLARY PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CATHETER SITE ERYTHEMA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CHEST DISCOMFORT			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CHEST PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
FACE OEDEMA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
GENERALISED OEDEMA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INFLUENZA LIKE ILLNESS			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
MALAISE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
OEDEMA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PERIPHERAL SWELLING			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
PYREXIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
THIRST			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VACCINATION SITE OEDEMA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
PELVIC PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VAGINAL DISCHARGE			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
CATARRH			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
DYSPHONIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
DYSPNOEA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPOXIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
IRREGULAR BREATHING			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DISORDER OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PHARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PNEUMONITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
STRIDOR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TACHYPNOEA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ATELECTASIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

AGITATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ANXIETY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BRUXISM			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DELIRIUM			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
IRRITABILITY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SLEEP DISORDER			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ABNORMAL BEHAVIOUR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Product issues			
DEVICE BREAKAGE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			

ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
AMYLASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ANTITHROMBIN III DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD CHLORIDE DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD POTASSIUM DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD THYROID STIMULATING HORMONE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD URINE PRESENT			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CANDIDA TEST POSITIVE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CARDIAC MURMUR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LIPASE INCREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
NOROVIRUS TEST POSITIVE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
OXYGEN SATURATION DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PLATELET COUNT DECREASED			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PROTHROMBIN LEVEL DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VITAMIN K DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LIMB INJURY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
POST PROCEDURAL SWELLING			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PROCEDURAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
THERMAL BURN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
UROSTOMY COMPLICATION			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
WOUND DEHISCENCE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CONTUSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Congenital, familial and genetic disorders			
FANCONI SYNDROME			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TACHYCARDIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
AMPUTATION STUMP PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DYSGEUSIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
HYPOAESTHESIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
MIGRAINE			

subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
MIGRAINE WITH AURA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NEURALGIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PHANTOM LIMB SYNDROME			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SEIZURE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SOMNOLENCE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TREMOR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DIZZINESS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PARAPARESIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 4 (25.00%)	1 / 2 (50.00%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

LEUKOPENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LYMPHADENOPATHY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LYMPHOPENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
THROMBOCYTOSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
EAR PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VERTIGO			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
ECZEMA EYELIDS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
EYELID PTOSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
OPSOCLONUS MYOCLONUS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PERIORBITAL OEDEMA			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PHOTOPHOBIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PHOTOPSIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ANAL INCONTINENCE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ASCITES			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
COLITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DENTAL CARIES			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

DIARRHOEA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
DYSPEPSIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ENTEROCOLITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HAEMATOCHEZIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LIP ULCERATION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NONINFECTIVE GINGIVITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ODYNOPHAGIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ORAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PROCTALGIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RECTAL DISCHARGE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

STOMATITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SUBILEUS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SWOLLEN TONGUE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLISTER			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DERMATITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DERMATITIS CONTACT			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DRY SKIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ECZEMA			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ERYTHEMA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PALMAR-PLANTAR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PERIORAL DERMATITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PETECHIAE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PITYRIASIS ROSEA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RASH PRURITIC			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SKIN DISCOLOURATION			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
URTICARIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DYSURIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
GLYCOSURIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HAEMATURIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYDRONEPHROSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NEPHROLITHIASIS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
OLIGURIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PROTEINURIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
URINARY INCONTINENCE			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
URINARY RETENTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPOTHYROIDISM			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
BACK PAIN			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	2
FLANK PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HAEMARTHROSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
MUSCLE SPASMS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
PAIN IN JAW			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
JOINT SWELLING			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
BACTERAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BRONCHITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CANDIDA URETHRITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DERMATOPHYTOSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
FUNGAL SKIN INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
GENITAL HERPES			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HERPES VIRUS INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

LARYNGITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LUNG INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
ORAL HERPES			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PARONYCHIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PHARYNGITIS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
PYELONEPHRITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SKIN INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
STAPHYLOCOCCAL			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TONSILLITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VASCULAR DEVICE INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VULVITIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	0 / 4 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
DEHYDRATION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPERKALAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPERNATRAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPERURICAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPOALBUMINAEMIA			

subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPOCALCAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPOKALAEMIA			
subjects affected / exposed	2 / 4 (50.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPERMAGNESAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 May 2015	Protocol was amended to include the following updates and clarification: There was an update to acceptable methods of contraception. Inclusion criteria were modified to include only children or young adults with tumor types that are known or expected to have PD-L1 pathway involvement. Patients being treated beyond radiologic progression were allowed to continue study drug treatment for 2 years. If a patient continued to experience clinical benefit beyond 2 years, the Sponsor could apply for additional approval from health authorities. The safety follow-up period was extended to 90 days. The initial dose of atezolizumab was changed to 15 mg/kg for all patients <18 years of age. Study drug treatment duration was changed to a maximum of 8 months. Patients continuing to experience clinical benefit at 8 months could continue study drug treatment with approval of the Medical Monitor. Pharmacokinetic outcome measures were modified to include blood draws during Cycle 4. Clarification made included: the first 5 patients had to be >= 2 years of age to ensure the safety and tolerability of children <2 years. There had to be at least 24 hours between the initial study drug doses of the first 5 patients. There had to also be at least 24 hours between study drug doses for the first 3 patients in each tumor type. Dosage information was modified to include patients <6 years. Clarifications regarding the timing of scheduled visits and assessments (every 6 weeks after Cycle 8) and thyroid testing (every 6 weeks throughout study). The endpoint for osteosarcoma was changed to CBRR, which was defined as percentage of patients who had an objective response or stable disease for at least 6 months. The exclusion criteria for lymphoma patients were modified to exclude patients with CNS lymphoma or leptomeningeal disease. The inclusion/exclusion criteria pertaining to CNS metastases were clarified.
15 October 2015	Protocol was amended to include the following clarifications: Management of gastrointestinal, dermatologic, pulmonary toxicity, hepatotoxicity, potential pancreatic or eye toxicity, and other immune-mediated adverse events was updated. Recommendations for early identification and management of systemic immune activation were updated. Clarification was added to specify that patients should not receive a live or live attenuated vaccine during study drug treatment and for 90 days following the last dose of atezolizumab. Clarification was added regarding the total amount of blood draw volume. Guidance was amended to specify that atezolizumab could continue while receiving radiation and the selection of lesions for radiation was clarified. Pregnancy testing was revised to be mandatory prior to every cycle for all female patients who have reached menarche. The number of patients to be enrolled in a tumor type cohort was set at a maximum of 40 patients in order to limit exposure to drugs with unclear efficacy.

21 October 2016	Protocol was amended to include the following key changes: INRC used in this study was modified from the original INRC publications; notations were added to the protocol to clarify the definition of measurable (evaluable) disease on CT and MRI scans for malignant lymph nodes. The protocol was modified to include patients with ATRT and RT based on significant clinical response seen in a patient in the non-rhabdomyosarcoma soft tissue sarcoma cohort. The safety monitoring and reporting period was clarified for SAEs, AESIs, and all other AEs in order to better focus on the most relevant safety information and to be consistent with the atezolizumab program in adult studies. The criterion excluding patients under treatment with investigational therapy (except specific cancer therapies) within 4 weeks prior to initiation of study drug was modified as the duration could be considered extensive in this impaired patient population. If required, patients could be evaluated on the basis of their grade of recovery of toxicity. The exclusion criterion referring to non-hematologic toxicity was modified to specify that long-term sequelae of prior treatment were not to be considered non-hematologic toxicity, but instead were required to be considered chronic medical conditions. The timing of various treatments prior to initiation of study drug treatment as specified in the exclusion criteria were amended. In addition, the study eligibility criteria were amended to allow enrollment of patients with a history of autoimmune-related hypothyroidism on a stable dose of thyroid replacement hormone and patients with controlled Type 1 diabetes mellitus on stable insulin regimen.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported